COVID-19 Journal Club

Clinical Cohorts

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Introduction

What is currently known about clinical cohorts in terms of comorbidities, symptoms, disease outcomes and treatment?

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Methods: selection criteria

- Peer-reviewed journals (e.g. JAMA, NEJM, Lancet)
- ≥ 100 COVID-19 cases
- English/Dutch
- Report disease outcomes (death/discharged)
- Report ICU admission

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Methods: search strategy

- Scanned all publications on LitCovid (mechanisms)
  - https://www.ncbi.nlm.nih.gov/research/coronavirus/docsum?filters=topics.Mechanism
- Checked EPPI-Mapper (health impacts)
  - http://eppi.ioe.ac.uk/COVID19_MAP/covid_map_v6.html
- Daily check of newest publications on LitCovid
- Results of this search strategy overlap with files in R folder of Epi
- Documenting in EndNote

Methods: table

- Table (in Dutch)
  - Intern analyses selected articles and fills in table in Excel
  - Two supervisors check table
- Multiple calls per week to discuss progress
  - Interpretation of data: similarities and differences between articles
  - Identification and interpretation of blind spots

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Methods: table parameters

- Article characteristics: author, journal, research type, research period
- Number of confirmed cases
- Demographics
- Comorbidities
- Symptoms: types, severity
- Disease outcomes: duration hospitalisation, ICU admission, death, discharge, complications
- Treatment: oxygen therapy (NIV & IMV), medication
- Sub-group comparison: multivariate analysis, descriptive

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Eerste auteur		Guan, NEJM	Wang, JAMA	Chen, Journal of Infection	Zhou, Lancet
Locatie	Land	China	China	China	China
	Regio	30 provinces	Wuhan	Shanghai	Wuhan
Type onderzoek		Retrospectief, multicenter (552)	Retrospectief, single center	Retrospectief, single center	Retrospectief, two-center
Periode onderzoek		11 december 2019 - 29 januari 2020	1 januari - 3 februari 2020	20 januari - 25 februari 2020	29 december 2019 - 31 januari 2020
Aantal cases		1099	138	249	191
Leeftijd (jaren)	Mediaan	47.0	56	51	56
	IQR	35.0-58.0	42-68	36-64	46.0-67.0
Man - n (%)		637 (58.1)	75 (54.3)	126 (50.6)	119 (62)
Rook historie - n (%)		158 (14.4)	NR	NR	11 (6)
Comborbiditeit - n (%)	Cardiovasculair	27 (2.5) (CHD)	20 (14.5)	55 (21.7)	15 (8) (CHD)
	Hoge bloeddruk	165 (15.0)	43 (31.2)	NR	58 (30)
	Longziekte/COPD	12 (1.1)	4 (2.9)	5 (2.0)	6 (3)
	Immunogecompromitteerd	2 (0.2)	2 (1.4) (HIV)	NR	NR
	Diabetes	81 (7.4)	14 (10.1)	NR	36 (19)
	Totaal	261 (23.7)	64 (46.4)	90 (36.1)	91 (48)
Symptomen	Koorts (38 graden of hoger) - n (%)	548 (59.2)	136 (98.6) (NS)	217 (87.1) (NS)	180 (94) (> 37.3 graden)
	Hoesten - n (%)	745 (67.8)	82 (59.4)	91 (36.5)	151 (79)
	Keelpijn - n (%)	153 (13.9)	24 (17.4)	16 (6.4)	NR
	Myalgie - n (%)	164 (14.9)	48 (34.8)	NR	29 (15)
	Sputum - n (%)	370 (33.7)	37 (26.8)	NR	44 (23)
	Misselijkheid en/of overgeven - n (%)	55 (5.0)	Misselijkheid 14 (10.1); overgeven 5 (3.6)	NR	7 (4)
	Diarree - n (%)	42 (3.8)	14 (10.1)	8 (3.2)	9 (5)
	Kortademigheid - n (%)	205 (18.7)	43 (31.2)	19 (7.6)	NR
	Neusklachten - n (%)	53 (4.8)	NR	17 (6.8)	NR
	Buikpijn - n (%)	NR	3 (2.2)	NR	NR
	Mild ziekteverloop - n (%)	926 (84.3) (niet-ernstig)	NR	NR	72 (38)
	Ernstig ziekteverloop - n (%)	173 (15.7)	NR	NR	66 (35)
	Kritiek ziekteverloop - n (%)	NR	NR	NR	53 (28)
Ziekteverloop	Dagen tussen eerste symptomen en ziekenhuisopname - mediaan (IQR)	NR	7.0 (4.0-8.0)	4 (2-7)	11 (8-14)
	IC opname - n (%)	55 (5.0)	36 (26.1)	22 (8.8)	50 (26)
	Dagen tussen eerste symptomen en IC opname -mediaan (IQR)	NR	10 (6-12)	8.5	12 (8-15)
	Dood - n (%)	15 (1.4)	6 (4.3)	2 (0.8)	54 (28.3)
	Ontslagen uit ziekenhuis - n (%)	55 (5.0)	47 (34.1)	215 (86.3)	137 (71.7)
	Nog opgenomen in ziekenhuis	1029 (93.6)	85 (61.6)	32 (12.9)	0 (0)
	ARDS - n (%)	37 (3.4)	27 (19.6)	8 (3.2)	59 (31)
	Vasopressie/septische shock - n (%)	12 (1.1)	12 (8.7)	NR	38 (20)
	Acuut nierfalen - n (%)	6 (0.5)	5 (3.6)	NR	28 (15)
	Acuut hartfalen - n (%)	NR		NR	33 (17)
Behandeling	Invasieve mechanische ventilatie - n (%)	25 (2.3)	17 (12.3)	NR	32 (17)
	Niet-invasieve mechnische ventilatie - n	56 (5.1)	15 (10.9)	NR	26 (14)
	Niet mechanische ventilatie	454 (41.3)	106 (76.8)	NR	41 (21)
	Antivirale medicatie - n (%)	393 (35.8)	124 (89.9)	NR	41 (21)
	Corticosteroiden - n (%)	204 (18.6)	62 (44.9)	32 (12.9)	57 (30)
Subgroep vergelijking	Multivariaat analyse	NR	NR	Hogere leeftijd onafhankelijk geassocieerd met IC opname.	Hogere leeftijd, hogere SOFA score, en d-dimeer > 1 µg/ml onafhankelijk geassocieerd met overlijden.
	Beschrijvend	Ernstig zieke patiënten waren ouder (verschil 7 jaar) en hadden vaker 1 of meer comorbiditeiten dan niet-ernstig zieke patiënten.	Patiënten op de IC significant waren ouder (verschil 15 jaar), en hadden significant vaker comorbiditeit en symptomen dan patiënten die niet op de IC lagen.	NR	Overleden patiënten waren ouder (verschil 17.0 jaar), en hadden vaker 1 of meer comorbiditeiten en complicaties dan ontslagen patiënten (allemaal significant).

Results

- Abstract + title screening: 22 articles
- Full-text screening:
  - 13 articles excluded: limited disease outcome data; no IC data
  - 9 articles included
- 8 articles general clinical cohorts
- 1 ICU cohort

- Countries: China, Italy, and the Netherlands
- All retrospective
- Single center, multi center (range 2-552)
- Follow-up period: range 3-7 weeks

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Results: general clinical cohorts (1)

Demographics & comorbidities

- Confirmed COVID-19 cases: range 136-1099
- Median age: range 41.2-72 years
  - Association between age and disease progression
- Majority male
- Comorbidities: hypertension (11.2-48.0%), cardiovascular (2.5-44.0%), diabetes (5.1-23.0%), lung diseases (0.4-44.0%), immunosuppressed (0.4-16.0%)
  - Highest proportions all from Dutch cohort (Elisabeth-Tweesteden ziekenhuis)
  - Association between comorbidities and disease progression

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Big range in percentages of comorbidities, because some studies report more specific diseases such as coronary heart disease, COPD, and HIV, whereas other use a combination and classify it as cardiovascular, lung diseases, immunosuppressed.

Results: general clinical cohorts (2)

Symptoms

- Most common symptoms: fever, (dry) cough, sore throat, myalgia, sputum production, shortness of breath, GI symptoms, nasal complaints
- Severity of disease
  - Mild: 38.0-93.3%
  - Severe: 6.0-26.8%
  - Critical: 0.8-28%
- Different definitions of severity: respiratory rate ≥ 30 beats/min, mean oxygen saturation ≤93%, PaO2/FiO2 ≤ 300 mm Hg

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Ratio of arterial oxygen partial pressure to fractional inspired oxygen

Results: general clinical cohorts (3)

Disease outcomes & treatment

- ICU admission: 1.4-29.6%
- Death: 0 – 29.8% (only 1 study with definite outcomes: 28.3%)
- Discharge: 5.0 – 86.3% (only 1 study with definite outcomes: 71.7%)
- Still hospitalised: 6.5 – 93.6%
- Complications: ARDS, septic shock, acute kidney failure, acute heart failure

- Oxygen therapy: NIV (0.6-30.3%), IMV (0.8-19%)
- Medication: antiviral (21.0-100%), corticosteroids (9.4-44.9%)

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Lowest ICU admission found in the "young" cohort (<60 years).
Complications are not very common.
Wide range of antivirals (oseltamivir, interferon alfa, lopinavir/ritonavir, arbidol)
Limited info on dose of corticosteroids

Conclusion

- Age and comorbidities associated with severe disease progression (ICU admission, death)
- Many single centre studies
- Short follow-up periods (limited disease outcomes)
- Progression after discharge unknown: e.g. persistent positive PCR
- Further research to determine whether comorbidities are independently associated with COVID-19 infection
- Further clinical cohort research for atypical presentation of disease: e.g. skin abnormalities, neurological abnormalities, clotting disorders

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Questions/discussion

- What about other literature websites? E.g. PubMed, Embase
- Could we put this table online together with a written description?
  - Do we need to inform people abroad about our work?
- What about primary care (eerstelijnszorg)?
- Overlap between primary care and asymptomatic cases and/or children/pregnant women. Include in our cohort research or different research?

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